

Neural Mechanisms of Audition

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YOUR REVIEWER has been instructed to deal with his subject matter in a comprehensive, analytic, critical manner, "setting forth the present status of our knowledge, making generalizations for which the collected data are adequate, and pointing out gaps in factual knowledge." He has approached this task with the viewpoint that what we know about hearing rests upon the threefold base of psychophysics, neuroanatomy and neurophysiology. Hearing is in the beginning a problem for psychology because the precise measurement of what men and animals discriminate about sounds is at the same time a definition of the phenomena for which the other two disciplines are to uncover neural correlates. Neuroanatomy is called upon to provide the data from which emerge suggestions and controlled speculations on what structures might be involved in the hearing process, and these, when integrated with the data of neurophysiology (with significant assistance from biophysics and acoustics at least), can be expected to lead to the common goal, namely a simple, rational and adequate set of neural correlates for auditory experience. No one discipline can accomplish all this alone.

Audition being a large subject matter, some limits must be placed upon any discussion of it. This review concerns itself mainly with the neural basis for the detection and discrimination of tones, a function loosely subsumed under the term *pitch* applied to the human auditory experience. History shows that much thought has been devoted to the question of what goes on in the brain as people achieve their analysis of tones, and of the many subjective attributes of tones—pitch, loudness, brightness, volume and density at least (14)—the pitch problem has always occupied a pre-eminent position. This review continues the tradition. With respect to what is omitted, two recent books (149, 166) competently present the basic facts of audition and, for those who wish to go even further, ample suggestions for further reading will be found in a recently published 5500-item bibliography (11).

PSYCHOLOGICAL CONSIDERATIONS

In very general descriptive terms, the pitch experience in man may be said to have three main aspects, each presenting its special problems for explanation. First, there is the simple fact that if we listen to a single pure tone we hear it. How is it that a regular train of sound waves striking the eardrum ultimately arouses any sensation at all? The remarkable fact that such physical vibrations become transmuted into the experience of tone may be commonplace observation, but its adequate explanation certainly constitutes our primary challenge.

Secondly, if two pure tones are presented, one after the other, we have two different pitch experiences. Even when the difference in frequency is made very small, the experiences remain distinct. What mechanisms are at work when the organism detects these slight physical differences in the sound? Presumably some crucial changes in neural activity underlie this ability and the task of achieving common agreement as to what these may be represents another of our goals.

When we examine the experience of listening to two tones sounding together, the third problem poses itself. Physically such a stimulus is a single complex and we may hear it that way. Yet, if we chose to do so, we listen to one of the tones and essentially disregard the other. How is the complex wave analyzed into its simple components, and how, furthermore, does the auditory system suppress one product of the analysis and not others? The answer here must include not only the different central effects of two tones but also, and more importantly, the mechanism by which the observer may direct his 'attention' to only one of them. Unless we listen we may fail to hear, and so the active process by which the hearer 'listens,' or focuses his capacity to make auditory discriminations, is a further subject for study.

These problems of pitch, as just defined, are peculiar to man, for no other animal can describe his subjective experiences as he listens to a single tone, or call one tone 'higher' than another in pitch, or report upon the results of attending to one tone in the presence of many. Yet most animals behave in nature, and can be taught to behave in experimental situations as if they too could distinguish between tones, and while this behavior is certainly not equivalent to the pitch dimension of auditory experience in man, as psychologists have frequently stressed (see, e.g. 14), it seems clearly related to it. As the reader will discover, the present discussion will have less to do with pitch than with the mechanisms for frequency detection and discrimination. Most experiments that pry into the ways of the nervous system are feasible only in animals, and so we must assemble here whatever we have of the neural correlates of the stimuli that in man would be expected to produce the pitch experience.

Receiving Organism. It will be useful first to examine the proposition that the pitch experience is common to, and essentially similar in, different human beings. The ability to perceive frequency and frequency difference is a question to which Seashore addressed himself repeatedly during his studies on musical talent in man. He (141, 142) and others (171) have demonstrated without question that people vary widely in this ability, and the well-known tests for musical aptitude include the measurement of pitch discrimination as an important item (19, p. 259). Intelligent adults may be utterly incapable of distinguishing one tone from another. There has been a lively controversy over whether such a deficiency can be corrected by practice and learning, Seashore contending not, while others have taken the opposite viewpoint. The evidence seems now to favor those who hold that pitch judgments can be learned, for striking improvements have been recorded in both children and college students when they are properly trained in the pitch perception task (171).

It is probably safe, therefore, to make the general point that the pitch experience in man results from a unique combination of an inborn capacity to analyze the difference between tonal frequency, and the acquired skill in doing so. If this is so, our search for neural correlates can proceed along two lines. First we must uncover the neurological *sine qua non* for the pitch experience, and second, we must discover those neural processes through which that experience may achieve its maximal expression. Pitch perception is not an automatic, invariable consequent of tone stimulation like, for example, the reflex eyeblink following a sudden loud sound or bright light. It is a function for which a neurological basis is provided by nature, but each individual may apparently use it or not (attention), or cultivate it or not (learning) as he will. Our attention will be directed here at what has been called the neurological basis provided by nature since we have almost no data at present on the other points.

Consideration of a well-known abnormality of pitch experience, diplacusis, provides some useful general information about the native neural equipment required for pitch perception. The pitches perceived in each of the two ears, interestingly enough, need not be the same. Normal subjects may report a significantly different pitch experience to the same tone if this is delivered to first one, then the other ear (73, 152, 166). This diplacusis phenomenon can become very marked when there is severe unilateral hearing loss of a temporary (30, 137) or permanent (98) nature. The ear with the loss displaces pitch upward when the loss is for lower frequencies (below 3000), downward when the loss is for higher frequencies (above 5000), but there is no displacement when the loss is in the 4000 cps region (137). When present, diplacusis is most marked with faint tones, tends to disappear as intensity rises, and may be entirely absent at high levels. The available facts make it likely that some deficiency in neural inflow from one cochlea is the fundamental explanation for diplacusis. This deficiency, furthermore, is gradually overcome as the sound becomes more intense. The analysis performed at the cochlea, finally, is critical for the process by which tones are heard and differentiated, but it is only a part of that process for if the abnormal ear should put out a distorted pattern of impulses, the central nervous system will still achieve a pitch sensation, albeit an erroneous one. Thus the understanding of what constitutes the normal undistorted pattern transmitted from the cochlea at various levels of intensity, and the answer to the questions of where and how the central nuclei deal with a pattern (whether it is a normal one or not) appear to be our two major problems.

A brief examination of the ability of lower forms to discriminate frequencies may further assist us in the attempt to define the native neural equipment demanded for the pitch experience. Restricting ourselves to fish and birds, it is clear that both these forms possess remarkably good hearing for tones. Some fish have an upper limit of around 1000 cps (33-35), but those possessing a swim bladder and Weberian ossicles may hear tones many octaves higher in frequency (42, 43). One of the latter, the minnow, perceives tones up to around 7000 cps, and shows a difference limen for frequency of at least 3 per cent between 400 and 800 cps (35). As compared to man, therefore, fish probably hear over a somewhat narrower range, and detect differences between tones less well; yet they do this with a most rudimentary auditory system (74).

Birds, as might be supposed from the behavior of forms like the parrot, are capable of making very fine discriminations between tones (76). Some of them hear frequencies as low as 40 and as high as 20,000 cps. Their differential frequency sensitivity is reported to be 0.3 per cent in the region of 1000 cps. Knecht concludes that in respect to both audible range and ability to discriminate frequencies the bird is not significantly inferior to man, and in its ability to retain or 'remember' a frequency difference, it may actually surpass him.

From even a cursory summary of the behavior of other vertebrates toward tones two important points emerge. In the first place, neither the range of heard frequencies nor the ability to discriminate between them can be related in any simple way to the degree of development of the peripheral auditory apparatus. In particular, a cochlea developed to the mammalian degree of complexity is obviously not necessary. Fish have no basilar membrane (indeed, they have no cochlea at all) and the organ of Corti of birds lacks the rods of Corti and certain other of the mammalian refinements (4, 129). Furthermore, the auditory tracts and nuclei of these lower forms, as far as these are understood (74), compare unfavorably in size and in degree of

organization with the system in cat or man. The bird, for example, is deficient in certain structures thought by some to be necessary for refined discrimination between tones (e.g. there appears to be no differentiation of internal as opposed to external haircells and no well-defined auditory cortex exists). If we make the assumption that the neural mechanisms underlying tone reception are similar throughout the phyletic scale, then the fact that the fish, with its primitive auditory neurology and no basilar membrane at all, may display better frequency discrimination than some of the people Seashore examined argues strongly for the viewpoint that both the requisite neural equipment and the interactions that go on within it are relatively simple and uncomplicated.

Effective Stimulus. The pitch experience is related principally to the sound frequency impressed upon the ear. Normal persons report a pitch experience for all sine waves between about 20 and 20,000 cps in frequency. Characteristically they call the pitch 'low' when the sound wave-length is long, and 'high' when it is short. These basic facts and a galaxy of related ones have been known for a long time and are adequately described and discussed in the literature (14, 151, 166).

A pitch experience can however be aroused by nonsinusoidal stimuli also. Noise, when regularly interrupted 40 to 200 times/sec., sounds to most persons as if it had pitch, and they match the interrupted noise to a tone of corresponding frequency (97). This fact along with others (139, 151) has led to the concept of a dual mechanism for pitch, the one depending upon the *periodicity* of the neural consequences of stimulation (at frequencies below 300/sec.), the other upon the *place* where those effects occur (for frequencies above 300/sec. at least). This possibility is currently being discussed (54, 80, 151) but does not yet seem to be resolved.

The differential frequency (and pitch) threshold has also been carefully studied and described. Most people readily perceive the change from one sound frequency to another and good subjects can detect very small changes indeed. According to one set of determinations (143), a variation of 2 or 3 cps is detected at frequencies up to about 1000 cps, while above 1000 cps the differential threshold is a constant fraction (about 0.3%) of the stimulus frequency. Other authors (136) report much smaller values than this. It has been repeatedly emphasized that the method used to make the differential threshold measurements is an important determinant of the results that will be obtained (63, 96, 151) but this fact is not explained in neural terms.

The intensity level at which a tone is presented also plays a significant role in the pitch experience. Pitch perception and the differential pitch threshold are best at high intensities, relatively poorer at low intensities and apparently entirely absent within 2 to 5 db of threshold (the 'atonal interval'; see 64, 103, 117). The influence of intensity may also be encountered when pitch matches are made between a fixed tone and one of the same frequency that varies in intensity. Pitch tends in most subjects to drop with increasing intensity if the frequency is below about 1000 cps and to rise if frequency is above about 4000 cps. Minimal pitch change occurs with tones around 2000 cps (99). The extremely wide variation among subjects in such an experiment is unexplained.

Pitch perception, finally, is also related to the duration of the tone being presented. 'Tones' can be so short (less than 6 msec.) that little if any pitch is attributable to them. When tones last as long as 12 or 15 msec. most subjects can assign pitch to them. As duration increases beyond this value the pitch becomes increasingly more firmly established, but for some tones, particularly those of low frequency, some uncertainty in fixing the pitch is still present at a duration of 100 msec. (36, 103, 165).

Recapitulation. From the discussion of the adequate physical stimulus, the pitch experience is seen to depend primarily upon the frequency of stimulation, but it is related importantly to both intensity and duration also. Pitch does not emerge instantaneously, nor is it a stable and constant aspect of all tones having the same frequency. Instead, subjects must listen to tones for a relatively long time at relatively high intensities before they firmly attribute precise pitch characteristics to them.

These facts, converted into gross neurological terms, imply that pitch depends upon the involvement of rather large portions of the auditory system, for relatively long times, and in particular ways. Near the threshold, where neural events evoked by tones are presumably minimal, an experience related uniquely to tonal stimulation is weak or absent; at increasingly higher intensities, as neural perturbations presumably continuously increase in extent and complexity, the experience becomes increasingly more precise and consequently easier to measure. The basic neural processes for both pitch and frequency discriminations seem, then, to come into existence only after minimal central spatial and temporal conditions are satisfied; increases in both these factors provide, up to a limit, the conditions for greater exactness in performance. The basic mechanisms, finally, are present even in lower forms having what looks like primitive equipment set aside for the task. With these points as guides we may now look into the anatomical and physiological studies for relevant correlates.

ANATOMICAL CONSIDERATIONS

The great neuroanatomists of the turn of this century defined a collection of nuclei and tracts that have come to be known as 'the auditory pathway.' Cajal's diagrams (21, 22), which are still published without essential change, show cochlear impulses to pass via the cochlear nuclei, superior olive, lateral lemniscus, inferior colliculus and medial geniculate to the auditory cortex. His conceptions have in general and in most details been repeatedly confirmed by physiological experimentation (2, 138). There can be no question that this classical cochleo-cortical pathway is a major route by which acoustic stimuli make their marks upon the nervous system, and that interactions among the neurons comprising this pathway hold the key to many auditory problems. A summary of our knowledge about these structures will be presented shortly.

Before doing so, however, it will be well to describe certain other pathways, some unknown to the classical anatomists, that also clearly deal with acoustic impulses. These pathways are being currently defined by active investigation, chiefly upon animals; they deserve our consideration because of their potential importance in the processes of hearing, including the perception of frequencies.

Auditory Connections With the Cerebellum. In 1944 Snider and Stowell (145), having pursued an accidental discovery that auditory stimuli evoke responses from the cerebellum of cats under chloralose anesthesia, demonstrated the existence of an auditory pathway from cochlea to cerebellar cortex. Electrodes upon the vermis of the cerebellum show responses to be aroused there by clicks and by light flashes as well (13, 145). Furthermore, electrical stimulation of this region produces recordable responses in the auditory areas of the cerebral cortex.

In addition to these ascending pathways, a descending system to this same cerebellar region is demanded by the experiments of Hampson (62), who has shown that

when those cerebral cortical loci from which sound and light arouse responses are themselves stimulated electrically, the vermis becomes activated. Snider's summary of these findings (144) demonstrates the need for the following additional acoustic pathways: a cochleo-cerebellar, for which connections have been described (105), a cerebello-cerebral, and a cerebro-cerebellar. While the puzzle of what these cerebellar pathways have to do with hearing remains to be solved, it has thus far been established that extirpation of the vermis, in conjunction with widespread cortical removals, is without effect upon frequency discrimination in the cat (93). Presumably the joint representation of the eye and ear at the same spot in the vermis is an important clue.

Auditory Reticular Pathway. The publications of Magoun's group (40, 41, 84, 85, 91, 147, 148) point to the existence of another hitherto unrecognized route by which impulses can pass from the ear to the cortex. The basic experimental observation is that cats with transections of the classical auditory pathway at the midbrain level can be readily aroused from sleep by sounds. Since only the central midbrain tegmentum is spared by such an operation, the inference that the auditory impulses are conveyed by way of the midbrain reticular formation appears inescapable. Presumably auditory collaterals enter the ascending reticular formation at the medullary levels, but where they do so is largely a matter of conjecture (see below for discussion). The cerebellar pathways just referred to are probably not involved, since decerebellation in addition to section of the main auditory pathways does not prevent the awakening reaction. The question of where rostral connections to the cortex are affected is similarly not settled. Nevertheless, the physiological evidence clearly supports the postulation of an ascending auditory pathway, in parallel with the classical main afferent one, whose course is through the reticular formation.

Recurrent Auditory Pathways. In the widespread preoccupation with the classical afferent pathway between cochlea and cortex, the numerous anatomical reports of a parallel descending system originating in the nuclei along the cochleo-cortical pathway have curiously received little attention. It is true that many of these reports are based upon the fickle and sometimes treacherous Marchi degeneration technique, and it would perhaps be unwise to place too much confidence in the unsupported observations of a single worker. However, since the time of Held (65) observations on one animal or another have pointed to the existence of pathways from cortex to medial geniculate body (22, p. 290, 31, 93, 106, 107, 114, p. 59), and inferior colliculus (4, p. 274); from medial geniculate body to the superior colliculus (1), lateral lemniscus (1, 109), and trapezoid body (1); from the inferior colliculus to the lateral lemniscus (65, 108); and from superior olives to cochlear nuclei (65) and the cochlea itself (4, p. 274, 124, 125, 127). Finally the dorsal cochlear nucleus is known to receive a considerable number of so-called centrifugal fibers not from the auditory nerve but from a source whose origin has not been established (88, p. 339).

Of all these recurrent paths, the olivo-cochlear tract described by Rasmussen (124, 127) is perhaps the most firmly established. Originating from cells near the superior olivary complex it ascends to the floor of the fourth ventricle, decussates, passes over the restiform body and leaves the medulla with the contralateral vestibular nerve (in cat). The fibers then enter the Oort (cochleo-vestibular) anastomosis, pass into the modiolus, and become distributed as the modiolar spiral bundle in the cochlea. The ultimate distribution of these fibers may well be the internal hair cells, as has been repeatedly claimed (12, 39, 119-121), but Rasmussen still reserves judgment on this point (127). In any event a crossed efferent pathway into the cochlea

has clearly been demonstrated. Earlier anatomists saw and described its various parts: The olivary peduncle and Cajal's 'crossed bundle of the vestibular nerve' (113) are its representative in the medulla, while Oort's anastomosis (125) and the internal spiral fibers in the cochlea (39, 89, 119-121, 125, 127) are its peripheral portions. It is possible that at least some of the 'vestibular' fibers that Winkler insisted accompanied the auditory ramus (see 74 for discussion) may, instead, have been the components of this afferent bundle. The bundle has been described in the monkey (6, p. 138), and may be presumed to exist wherever the bundle of Oort occurs.

In a current series of experiments upon these descending tracts, (101, 126) the Nauta silver method is being used to trace degenerating auditory axons in the recurrent system. Lesions have been made in cats at the auditory cortex, medial geniculate, inferior colliculus and superior olivary levels, the subsequent axonal degenerations have been traced, and the cells upon which these axons end have in many cases been identified. The results abundantly confirm the earlier observations that important recurrent pathways exist, and the following have thus far been identified: cortico-medial geniculate (*pars magno cellularis*), geniculo-inferior collicular, geniculo-lateral lemniscal, inferior colliculo-superior olivary (bilateral), and superior olivo-dorsal cochlear nuclear (bilateral). While, as has been pointed out, unassailable evidence that the olivo-cochlear efferents actually end around hair cells in the cochlea does not yet exist (127), this pathway may perhaps provisionally be considered to represent the final link in an auditory pathway that descends from the auditory cortex to the end-organ. Considerable support for this idea is provided by the observation (126) that lemniscal lesions caudal to the inferior colliculus result in heavy terminal degeneration on cell bodies dorso-medial to the accessory olives of the same side. It happens that this is precisely the locus of the cells giving rise to the olivo-cochlear bundle.

Physiological evidence on these descending pathways is meager. Hampson's need (62) for cortico-cerebellar connections has been commented upon earlier. The claim that cortico-geniculate connections have been demonstrated (23) has been disputed (18, 52). The existence of efferent connections to the cochlea has been inferred from some preliminary experiments (53). This brief list assembles virtually all the available physiological material.

It is unlikely that these descending fiber systems—some reasonably powerful, some weak—perform no function in audition. What this function might be will unfortunately continue to remain entirely speculative until more anatomical and physiological data become available. One can hazard a guess, however, that the solution of certain problems of hearing resides as much in the understanding of the function of these descending neural pathways as in the knowledge of the ascending ones.

Classical Auditory Pathway. The summaries that follow are intended to present the main anatomical features of the various nuclei that comprise the classical auditory pathway in mammals. They rely heavily upon Cajal's well-known descriptions (21, 22) and those of recent American investigators to which the reader is referred for complete details. Stress has been placed here upon those facts that have, or may have, relevance to the problem of tonal frequency analysis, but since it is by no means certain what these relevant facts are, some material pertaining to hearing in general is inevitably included.

Before passing to the descriptions themselves, a few general references may be useful. Those interested in the comparative aspects of the auditory pathways will find the accounts of Kolmer (4), Kappers *et al.* (74) and Papez (114) rewarding. This

system appears to be unusually easy to trace through the phyletic scale. A recent study of the development of the system in man has been presented by Cooper (26). Chow (25) has counted the cells in each of the nuclei from cochlea to cortex in the monkey; from these data the way the pathway expands as it ascends can be estimated. If the number of auditory nerve fibers is called 1 (its actual value is about 30,000, ref. 123) the cochlear nucleus gives rise to about 2.0 efferents, the superior olivary and lateral lemniscal nuclei 2.5, the inferior colliculus 13, the medial geniculate 14, and the auditory cortex 340. These estimates should prove of considerable assistance to those who view the auditory system from a statistical basis. Reference should also be made to the studies of v. Soubiron (146); his work has been done chiefly upon human pathological and embryological material.

Cochlear neurology. Anatomical relations between the hair cells and their neurons in the cochlea can be discussed either by concentrating upon the hair cell, inquiring into how the neuron ends upon it, the number that do so, etc. (see, e.g. 28, 37, 75), or by describing the various systems of neurons that exist, plotting their course and distribution and specifying the number of hair cells upon which a given neuron ends. The latter viewpoint is the one to be taken here. It must be assumed that the reader is familiar with the general morphological details of the mammalian cochlea, for space limitation precludes such a description here (see 150, 166).

The hair cells, internal and external, come into relation with at least four systems of neurons (4, 21, p. 776, 39, 89, 129, 157). *Radial fibers* make contact mainly, if not exclusively, with internal hair cells. Each fiber is related to no more than several hair cells, and several fibers may innervate each hair cell. This fiber system, which exhibits an almost direct connection between a hair cell and a neuron, affords a clear basis for the hypothesis of a one-to-one relation between a place on the basilar membrane and a place within the central nervous system. *External spiral fibers* are distributed practically exclusively to external hair cells. Before leaving the organ of Corti, some of them have made contact with hair cells throughout 2 or 3 mm. of the cochlea at least. Most of them enter the ganglion of Corti at a point more apical than the hair cells they innervate. Some neurons are related to one hair cell, others to very many hair cells (66); this arrangement thus provides for both a direct and a diffuse relationship between the basilar membrane and the central nervous system.

Internal spiral fibers are distributed 'almost exclusively' (39, 89) to the internal hair cells, and each fiber innervates an unspecified, but probably large, number of them. Of very fine caliber, these internal spiral fibers proceed spirally in both the basal and apical directions, at first within the modiolus (where they are called spiral bundles or spiral fibers of the ganglion), later beneath the internal hair cells (89). Recent intensive study of this complex (12, 39, 119-121, 125, 127) strongly suggests an efferent function for at least half (127) of them. Whether the remainder are afferent or efferent has not been established. The efferent fibers are the cochlear extension of the olivo-cochlear tract which, arising near the contralateral superior olive, makes its way across the dorsal medulla to enter the cochlea as the bundle of Oort (125). They may end near (127) or upon (39) the internal hair cells, which, interestingly enough, possess two morphologically different nerve endings (75).

There is a rather poorly defined group of internal spiral fibers at the apex of the cochlea that may belong to none of the systems thus far discussed (21, p. 776, 128). A tunnel spiral bundle also exists; it may be part of the internal spiral system (166, p. 225). In addition Cajal saw and described neurons having an apparent central origin that terminate among the cell bodies of the spiral ganglion of Corti (21, fig.

325). These scattered observations are examples of the observations that do not at present fit systematically into the descriptions of the cochlear neurology.

The pressing questions today are the ones that have always faced the student of hearing: first, what in fact is the system of neural connections that exists in the cochlea, and second, what actions are produced in and what interactions occur among these neurons as the cochlea converts mechanical motion into the nerve impulses?

A few observations will point up the importance of further information on these matters. The anatomical facts clearly provide through internal (and a few external) hair cells a point-to-point, and through external (and some internal) hair cells a diffuse, relation between the basilar membrane and the central nervous system. The functional significance of these direct and diffuse anatomical projections is completely unknown. The internal hair cells at least, furthermore, could conceivably be influenced reciprocally by the central nervous system through impulses originating in or near the contralateral superior olive. Should the efferents perform such a function, the hair cell-auditory nerve junction would have to be viewed not only as the place where stimulus energy is converted into nerve impulses but also as the first locus where neural interactions may occur in the auditory tract. In addition to their differing innervation, internal and external hair cells are unlike in other ways that presumably are related to functional differences. External hair cells are essentially bathed in fluid while the internals are surrounded by supporting cells (59); the internals rest on bone, the externals on basilar membrane (90); and acoustic trauma is much more likely to destroy externals as compared to internals (137). These are all mechanical items whose significance remains to be settled. Progress toward solutions can be seen in the contributions of v. Bekesy (7, 8) whose latest report (9) upon the motion of the basilar membrane as this is observed under the microscope raises important new questions also. For example, he shows the hair cells to be capable of three kinds of motion. A hair cell located at the peak of the cochlear wave produced by a tone oscillates up and down in the direction of its long axis. At a higher tone frequency the same hair cell oscillates in the direction of its short axis. At a lower frequency it swings like a pendulum with the region of its hairs being essentially fixed. Conceivably these three types of motion could affect the recipient neurons in different ways. The relation of these recipient neurons to the hair cells they innervate is being currently studied with electron microscope techniques (37). Some nerves end as simple buttons while others form clusters that cover an area of 4 to 5 μ applied closely to but not penetrating the hair cell membrane.

Cochlear nuclei. To the classic description of this nuclear complex by Cajal (21, p. 779) and Lorento de Nó (87, 88), the work of Lewy and Kobrak (79) and Niemer and Cheng (105) can now be added. The cochlear nuclei are divisible into a dorsal and a ventral group, each of these being further subdivided into smaller complexes having characteristic cell-types, afferent collateral endings and efferent connections (88). The dorsal cochlear nucleus is laminated, like the cerebral cortex, while the ventral is not. Morphologically this aggregate is "... even more complicated than the retina or olfactory bulb, which are, according to Cajal's description, the primary nuclei of highest differentiation in the nervous system..." (88, p. 336), and the diameters of its efferent fibers (via the trapezoid body) include both the largest and the smallest found in central pathways (21, 128). Without doubt, and despite the considerable efforts of the anatomists, we are in possession of merely the bare bones of the true morphological picture. Nevertheless, on some points reasonable agreement has been reached:

1) All afferents from the cochlea enter the medulla, bifurcate into rostrally and caudo-dorsally directed collaterals, and make synapses in each of at least 13 distinct subdivisions of the cochlear nucleus complex (4, 45, 55, 79, 88, 92, 159, 169).¹ Each cochlear fiber thus terminates upon a great many cells. It might be expected that the two afferent systems from the cochlea—the radial and the external spiral groups—

¹ We must here take notice of Stotler's insistence (153) that the cochlear nerve ends only in the ventral cochlear nucleus and sends no fibers to the acoustic tubercle.

would terminate differently in the cochlear nucleus; only one type of termination however has been described (88).

2) A remarkable orderliness is apparent in the distribution of the afferents. Fibers originating at the apex of the cochlea (where low tones excite: 7-9, 140, 156) bifurcate at the most lateral and inferior margin of the nucleus, while those from the base (high tones) do so most dorsomedially. Fibers from intermediate regions bifurcate at intermediate positions in a complex but systematic manner (79, 87, 88). Beyond the bifurcation point the collaterals preserve their relative positions up to the cells upon which they end, and hence, the apical part of Corti's organ is represented ventrolaterally, the basal part dorsomedially in the cochlear nucleus. Order is thus impressed upon the cells within this structure, and we can conclude that in some, if not in all, of its 13 subdivisions, the geographical (spatial) correlate for frequency established at the basilar membrane is repeated in the first central nucleus. In other words, the cochlea is 'unrolled' at the cochlear nucleus, not just once, but repeatedly. Physiological evidence for this has been reported (51).

3) Lorente de Nó differentiates at least 50 types of cells located in the cochlear nucleus complex (88). Many of these can be grouped into two categories on the basis of the morphology of the primary afferent terminations they receive. The ventral nucleus (of Lorente de Nó; anterior ventral of Cajal) illustrates both categories. Thin fibers break up into a diffuse plexus around certain cells, while thick fibers end by enveloping a substantial portion of the soma surface of others in the so-called end-bulbs (or calyces) of Held (see also 153). These endings have been termed, respectively, collateral and terminal synapses (21, 88, p. 340).

4) The known afferent supply to the cells of the cochlear nuclei includes the auditory nerve fibers; a powerful bundle of unknown origin to the dorsal group (the centrifugal fibers of Lorente de Nó, 88, p. 339); neurons with short axons that connect one subdivision with another (the regulator neurons of Lorente de Nó, 88, p. 338); and collaterals of recurrent fibers from the inferior colliculus (126). It is probably safe to assume that the whole story of the extra-cochlear afferents to the cochlear nuclei has not yet been told. Even so, the known afferent supply leads readily to the generalization that the cochlear nuclear complex is a mixing-pot into which impulses of diverse spatial and temporal origin converge and interact. A considerable analysis of the acoustic message must occur here in space (i.e. at the 13 subdivisions) and in time (since the various afferent routes differ in length of path).

The efferents from the cochlear nuclei have been concisely summarized (104) as follows: "*a*) The anterodorsal cochlear nucleus projects to the cerebellar auditory center (tuber vermis); *b*) the posterodorsal cochlear nucleus projects to the contralateral inferior colliculus; *c*) the dorsal part of the ventral nucleus projects to the opposite superior olive; *d*) the projection of the ventral part of the ventral nucleus remains uncrossed and terminates in the superior olive."

Superior olivary region. Cajal's very extensive description of the superior olivary nuclear mass (21, p. 795) is still the definitive one, but Stotler's recent contribution (153) marks a significant forward step. Currently at least five major subdivisions are recognized in the total mass; the superior olive proper (or the lateral S-shaped segment, 113), the accessory superior olive, the internal and the external pre-olivary nuclei, and the nucleus of the trapezoid body. Among the lesser subdivisions might also be included the nuclei of the lateral lemniscus. Still another is the group of cells located just medial to the accessory superior olive and above the nucleus of the trapezoid body giving rise to the olivo-cochlear (efferent) pathway (125). Cajal (21) may have them shown as part of the latter nucleus in his figure 344.

Afferents to the superior olive come mainly from the ventral cochlear nucleus (21, 105, 153), although the auditory nerve (see 153, p. 418, for discussion) and dorsal cochlear nucleus (74) have been said to innervate it also. Stotler's summary (153) describes these afferents in a clear and concise way. From more rostral regions a pathway descends to end in the region of the cells giving origin to the olivo-cochlear pathway (126).

The fine structure of these nuclei is extremely varied and interesting. Their afferents, having pursued orderly but complex paths, ultimately end with either collateral or terminal synapses as in the cochlear nucleus (21, 153). Unilateral innervation through end-bulbs of Held occurs in the nucleus of the trapezoid body (which Cajal thought might be a displaced portion of the ventral cochlear); its cells can be essentially deafferented when the contralateral cochlear nucleus is removed (153). In the accessory superior olive, on the other hand, each cell receives bilateral innervation, for removal of one cochlear nucleus produces only partial degeneration of its end buttons, and degeneration, furthermore, that is limited to the dendrite on the side of the lesion (153). This polarity at the synapse is only one of many unexplained curiosities of this nuclear mass.

Efferents from this cluster of nuclei are numerous and the existence of some, as well as full details on all of them, are still to be settled. The superior olivary region appears to be an important station in the main cochleo-cortical pathway since practically all (90-95%, see 105) of the output of the S-shaped segment is distributed equally between the two lateral lemnisci (but see 109), while the other nuclear groups send their fibers into the lateral lemniscus also (6, 125, 153, 172). It will be noted that each ear is thus abundantly represented bilaterally at this level.

A second major group of efferents is said to make reflex connections with the motor nuclei of the muscles of the eyes, middle ear, face, neck and body. The existence of such connections, shown by Cajal (see his fig. 362), has been denied (113, 153), but Yoshida (172) and Rasmussen (125) cite the medial parts of the superior olivary complex as containing their cells of origin, and v. Soubiron (146) has traced such connections to the III nerve in the human fetus.

Of considerable interest is the question of whether collaterals might enter the reticular formation at this level to provide an inflow into the reticular pathway to the cortex discussed above. Substantial connections that could serve this function have been seen by at least four competent observers (6, 21, 125, 172) but at least two have looked for but failed to find them (113, 153).

The final known group of fibers leaving the olivary region is the tract of Rasmussen, or the olivo-cochlear pathway, which arises medial to the accessory olive and terminates in the contralateral cochlea (*vide supra*). This tract was formerly called the olivary peduncle, and (by Cajal) the "crossed bundle of the vestibular nerve" (113).

Very little is known about what part if any the complex of nuclei described above might play in the detection of tones. They have, in the past, been thought to have important or even exclusively reflex functions, but recent anatomists insist they are primarily relay nuclei in the main afferent pathway (105, 113, 153). In cat and rabbit, where the complex is large in size, this region may be presumed to be functionally very important; in the primate the S-shaped segment at least is ill defined (153). The homologous nuclei in the bird seem simpler in structure than those of mammals (21, p. 831, 74). So far as is known, the superior olivary region has not been studied extensively by any physiological method.

Lateral lemniscus and its nuclei. Cajal's brief summary (21, p. 823) is to be sup-

plemented by more recent studies (6, 112, 125, 153, 170). The lateral lemniscus is made up of fibers from the contralateral cochlear nucleus (both dorsal and ventral, 125; only ventral, 153) and from the superior olivary region of both sides (see above, and 153 for details). Only the cochlear nucleus component seems to be interrupted by synapses in the nuclei of the lateral lemniscus (153). These nuclei, a dorsal and a ventral, are distinguishable on the basis of cellular morphology (21), and because collateral synapses predominate in the dorsal region while typical end-bulbs of Held form terminal synapses more ventrally (153). When viewed in cross section at the appropriate level the lateral lemniscus is seen to consist of a central cellular region surrounded by fibers; these fibers are collected, more or less, into bundles, so that all axons stemming from a particular source pass along together (125, p. 178, 153). Thus, as in so many other locations, an orderliness is discernible at this level also.

The lemniscus fibers end in the inferior colliculus (of both sides, according to most authors), the superior colliculus (22, p. 171) and the medial geniculate. Those stemming from the olives probably end mainly in the colliculus, while those that synapse in the nuclei of the lateral lemniscus probably project mainly to the medial geniculate. The lemniscal nuclei also send fibers to the reticular formation (153), thus affording a possible route through which the reticular pathway to the cortex might become activated by acoustic stimuli.

Inferior colliculi. This way station in the auditory pathway receives considerable attention from Cajal (22, p. 154) who recognizes three regions within it: a spherical main nucleus, a gray mass medial to this that joins with its fellow of the opposite side, and a smaller nucleus embedded among the arriving and departing fibers. He considered these structures to constitute an auditory reflex center, holding that the main central pathway essentially by-passes the inferior colliculus except for the collaterals it emits on its way to the medial geniculate bodies. It has however been suggested that the inferior colliculi perform an analysis of tones and can replace that of the auditory cortex (86).

Afferents arriving from the medulla are of two major types. Some (relatively few according to Cajal) lateral lemniscus fibers terminate in the inferior colliculus; these may end in one or more of its subdivisions. Other lemniscal fibers merely send one or more collaterals to the region; these likewise may penetrate more than one region of the colliculus. Still other afferents include a considerable number of fibers arriving from the subdivisions on the opposite side, and afferents from above (126).

Each of the subdivisions of the inferior colliculus contains at least two types of cells. These are differentiated on the basis of size, dendritic morphology, and apparent connections. Cajal's discussion (22, p. 155) includes many details about the dendrites, not the least interesting of which is a remarkable change in those of the large multipolar cells of the main nucleus that occurs shortly after birth. As for the ultimate distribution of various axons arising here he has much less to say, having been unable to follow their course over any long distance. It is clear, however, that rich connections exist between the cells of a given subdivision as well as with the other subdivisions of the same and opposite sides. The known distant connections include the major one, to the medial geniculate body, and lesser tracts to the superior colliculus and lower centers (via the tecto-spinal, pontine, bulbar and nigral tracts) (22, 74 p. 1069, 108). These latter are of some interest because they might afford opportunity for activation by auditory signals of the reticular pathway ascending toward the cortex.

Medial geniculate. Cajal's description (22, p. 284; see also 110) separates the medial geniculate into superior and inferior lobes of which only the latter is surely

assigned a role in audition. He further subdivides this inferior lobe into *deep* and *superficial* nuclei, a distinction much like that implied in the current terms *pars magnocellularis* and *pars principalis* applied to the medial geniculate of carnivores (130, p. 68, 131). An analogue of this nucleus is probably present in reptiles and birds (74, p. 1060; 111, fig. 247).

The chief afferent supply to the medial geniculate arrives via the lateral lemniscus and the brachium of the inferior colliculus. In Cajal's view axons present in the trapezoid body pass without interruption to the medial geniculate; more recent work (6, 112, 170) is practically unanimous in holding that relatively few such axons escape at least one synapse (at the nuclei of the lateral lemniscus, the inferior colliculus, or elsewhere) in their course from medulla to medial geniculate. Cajal distinguished two types of arriving fibers: thick ones, each terminating upon a considerable number of cells in the superficial nucleus (*pars principalis* ?), and thin ones, each ending with elaborate arborizations upon very many cells in the deep nucleus.

It is interesting to point out that Cajal also recognized a second system of afferents to the medial geniculate. Described in the mouse, these so-called centrifugal fibers descend, possibly from the cerebral cortex, to terminate in the inferior lobe.

A word is in order about the commissure of Gudden, a pathway shown in many textbooks as connecting the two medial geniculate bodies. Cajal clearly described it as arising from, and ending in, his nonauditory "superior lobe of the medial geniculate." Its other connections with the thalamus and tectum are not well understood (74). Ades (1) addresses the question of whether Gudden's tract has an auditory function, arriving at a negative answer. It would appear, therefore, that no clear interconnection between the auditory geniculate bodies exists, and that at the thalamic level there is no known opportunity for the main afferent pathways of the two sides to mix.

The fine structure of this nucleus has only in part been described. According to Rose (132, 134) who has reviewed the literature, the *pars principalis* consists of small cells, the *pars magnocellularis* of fairly large, densely packed ones. Cells of the *pars principalis* degenerate when their axon terminations in the cortex are removed; Rose (133, 135) describes the relatively restricted locus of such cell loss when various limited cortical areas are damaged.

The main neural outflow of the medial geniculate forms the auditory radiation which ascends in the internal capsule to its ending in the auditory cortex. In the radiation those fibers that terminate in a particular cortical locus pass along together (118), leading to the inference that if the cochlea should be 'unrolled' at the cortical level a similar conclusion can be drawn for the radiation also.

The question of whether the thalamic system just described is the only thalamic one involved in transmission of impulses aroused by tones has not been completely settled. Physiological studies (47, 52, 134) indicate the *pars principalis* to be the main thalamic representative of the auditory system; no function can as yet be surely assigned to the *pars magnocellularis*. Furthermore, other fiber systems to and from the medial geniculate exist, but what if anything they have to do with processing the neural response to tones is unknown. Discussions of these other tracts and nuclei (e.g. the tecto-cerebellar system of fibers and the parabigeminal nucleus) are on record (74, p. 1168; 112).

AUDITORY CORTEX

The vast literature upon the mammalian cortex has been recently covered in two succinct treatments of problems of major interest to us (44, 133). Lorente de

Nó's summary, while not specifically on the auditory cortex, is required reading for those who wish insight into its function, for he describes there the elementary cortical pattern common to all mammals. Afferents to the cortex are classified into three types: specific thalamo-cortical, nonspecific thalamo-cortical, and cortical association fibers. For the auditory pathway the specific thalamo-cortical afferent derives of course from the medial geniculate body; it ends mainly in *layer IV*, and to a lesser extent in *layer III*, through a remarkable collateral synaptic termination that must make contact with very many cells. The existence of the nonspecific thalamo-cortical fiber has not been verified in higher mammals, but in the mouse, where it can be seen in at least some cortical areas, it ascends as far as cortical *layer I*, giving off branches at all levels, but chiefly in *layer VI*. The thalamic origin of these fibers is unknown. One may speculate upon their possible relation to the previously discussed system ascending through the reticular formation (72); on the other hand those related to the auditory system could, conceivably, stem from the cells in the 'dorsal thalamus' cited (146, p. 242) as the origin of the axons that form the dorsal portion of the acoustic radiation in man. However, most questions related to the nonspecific auditory afferents must apparently remain, for the present, unanswered. The third type of afferent is derived from distant cortical cells of the same and of the opposite side. These association fibers terminate chiefly in *layers I* through *IV*, (but see 100, where the terminations are given as *I* through *VI*).

The cortical efferents are classified, in general, into association and projection groups. Fibers cross in the corpus callosum and some descend (as discussed above) to the thalamus; relatively little further is known about the auditory cortical efferents.

The understanding of the function of the cortex is complicated mainly by the presence there of neurons with short axons (Golgi Type II) of which three types are described. The interconnections of the terminations of these elements among themselves and with those of the afferent and efferent elements having long axons are treated briefly and lucidly by Lorente de Nó (44). Both he and v. Soubiron (146) stress the importance of these cells with short axons, the latter pointing out that if the auditory radiation is destroyed inconsequential change occurs in the fine structure of the cortex itself. For those interested in further details on the synaptic problems of the cortical neurons the work of Chang (24) may be useful.

Having dealt with the general problems of cortical organization we may now turn specifically to the auditory cortex and its relations. The available evidence here is meager for all forms except the cat and dog, and even for these animals the information is often incomplete. Most of the studies have been directed at answering one or more of the following questions: 1) what is the extent and structure of the 'auditory' cortex; 2) is it divisible into substructures; 3) what are its afferent and efferent connections; and 4) is the cortical organization topologically related to the basilar membrane? The present status of the answers to these questions can best be described by treating the available anatomical and physiological data together.

Discussion over the extent of the feline 'auditory cortex' continues, but with evidence that considerable progress has been made in recent years (15-17). The two publications (133, 135) that warrant careful study summarize the previous work and are authoritative on the cytoarchitecture of, and the thalamic projections to, the auditory cortex in the cat. The 'auditory area' is located upon the lateral surface of the hemisphere; its rostral, dorsal and caudal boundaries are, roughly, the suprasylvian sulcus while inferiorly it ends about at the level of the tip of the pseudo-

sylvian sulcus. Four subdivisions can be recognized within this area on the basis of cytoarchitecture. A central field, or first auditory area (also called AI) is bordered by the second auditory area (AII, below), the posterior ectosylvian area (Ep, behind), and the suprasylvian fringe sector (above). The medial geniculate (pars principalis) degenerates significantly only after removal of AI, and so its essential projection is to this cortical region. Since, furthermore, the degeneration is localized with small cortical lesions, and variable in location with different ones of them, it can be inferred that the projection is topologic. These authors were unable to ascertain the origin of the projection fibers to the other subdivisions of the cortex but discuss collaterals of the geniculo-cortical tract and fibers from other thalamic nuclei as their possible source.

The existence of a 'third' auditory area, AIII, was first demonstrated by physiological techniques in the dog (161). It lies rostral to the other subdivisions and within the confines of Somatic II (94, 95); it is a region, therefore, in which both sound and somatic stimulation will evoke responses. Its presence has been confirmed in the cat (17, 115; but see also 70).

The above brief summary of the extent of the feline auditory cortex stresses the points upon which agreement is reached and scarcely does justice to the problems that remain. Unquestionably useful detailed information will be forthcoming from the further experiments of Bremer on the *encephale isolé* preparation, of Lilly using multiple electrodes for simultaneous recording (82, 83), and of others.

On the question of whether the cortical representation of the basilar membrane is topologic, physiological studies on dog (160-164) demonstrate with unusual clarity that the cochlea is indeed unrolled in AI. Tunturi's results obtained with the strychnine technique are particularly striking. This drug when applied to a cortical area so sensitizes the underlying structures that afferent impulses arriving there evoke large distinctive spikes. Afferents that terminate elsewhere fail to produce that specific effect. Using strips (163) and 1 mm.² patches (164) of strychninized cortex in the middle ectosylvian gyrus of the dog, Tunturi has shown tones close together in frequency to be represented there in a narrow band. Low frequencies activate their bands in the more caudal portion of the gyrus, while progressively higher tones activate bands more rostrally located. Each band is about 8 mm. long. A supra-threshold tone, when applied to the contralateral ear, activates the whole of its band regardless of the intensity used. Tones to the ipsilateral ear, however, activate a restricted dorsal portion of the band when they are weak, and more and more of its ventral extent as their intensity is increased. Thus, for the dog, only frequency has a discernible spatial representation in contralateral AI, while both frequency and intensity are thus represented in ipsilateral AI. The situation in the cat may be similar, but the available information on this form does not yet warrant such a conclusion (50, 70). As to whether a tonotopic organization exists in the other subdivisions of the auditory area, the evidence is favorable, for AII at least, in both dog (160, 161) and cat (70).

Recapitulation. Out of the welter of details in the summaries just presented, certain main facts, or principles of organization, emerge for consideration. The first of these is the old but fully confirmed observation that a remarkable orderliness is to be found from one end of the auditory system to the other. At the cochlea, where tones of different frequency produce effects in different places, neurons are so connected to the internal hair cells (i.e. almost one-to-one) that this spatial correlate may be precisely preserved. In the auditory nerve, where the various fibers twist

about in a complex way, those from the apex of the cochlea do not mix indiscriminately with those from the base. At the point where these fibers bifurcate in the cochlear nucleus, those from the apex of the cochlea assume a lateral inferior position, while those having a progressively more basal origin bifurcate at progressively more dorsomedial locations. The ultimate terminations of these fibers, finally, are in nuclear submasses in some of which at least the cochlea is topologically represented or, in common parlance, unrolled. At neural levels higher than this, evidence from anatomy neither supports nor denies the topologic concept; it is simply non-committal. However, order is clearly present where it has been looked for as, for example, in the lateral lemniscus and medial geniculate. So far as it goes, therefore, anatomy provides a solid topologic relation between the basilar membrane and the auditory neural structures for those who wish to look into the question of whether a tonotopic relation exists also.

Having settled upon *order* as a prominent feature of the auditory anatomy, we must now concede that what looks like disorder or *diversity* is clearly a second major principle. This diversity expresses itself in various ways. We have seen how, throughout the medulla, terminal synapses (the end-bulbs of Held) predominate in some places while only collateral synapses occur nearby. This means that the relation of pre- to post-synaptic element is essentially one-to-one (or, perhaps better, few-to-one) in some nuclear regions but many-to-one (which usually means one-to-many also) in others. This repeats the situation known to exist at the basilar membrane, for there most internal hair cells bear essentially a one-to-one relation to their recipient neurons, while external hair cells, on the whole, fall into the many-to-one category. Thus, at the four earliest stations in the auditory pathway—the cochlea, the cochlear nuclei, the superior olivary complex and the lateral lemniscus nucleus—a recipient neuron is either very directly, or very diffusely related to its source of excitation. Whether similar diffuse and direct systems exist at higher levels also has apparently not been the subject of specific investigations. Nor is it at all clear that the neurons related one-to-one at, say, the cochlear nucleus are the direct antecedents of those similarly related in, say, the lateral lemniscus.

Another illustration of the principle of diversity is the multiple topological representations of the cochlea throughout the nervous system. In the cochlear nuclei where Lorente de Nó has identified some 13 morphologically different loci into which each auditory fiber finds its way, the cochlea is, so to speak, unrolled many times. Each cochlea is also unrolled at least once on both cerebral cortices, and at way stations in between.

A final example of the diversity under discussion is the multiplication of the pathways by which impulses aroused by tones may, at least theoretically, find their way from cochlea to cortex. Little can be said for or against the idea that the auditory path by way of either the cerebellum or the reticular substance participates in the reception and discrimination of tones. This question, which is probably worth asking, must simply be left open. However, when the physiological significance of the diverse routes through which the end organ activates the nervous system becomes clear we will have made a substantial step toward understanding the neural mechanics of tone perception and discrimination.

A third principle of organization, worthy of only brief mention at this time, is the arrival, at each nuclear station, of fibers from auditory stations lying both above and below the one in question. Most descriptions of auditory neuroanatomy concentrate upon the fibers that arrive from below. However, the recurrent, or descending,

fiber systems described in fragments by classical anatomists and currently being re-examined with the newer anatomical methods, provide in principle at least the means by which the events at a given locus in the auditory brain may be influenced not only by what goes on at the cochlea but also by what transpires at higher levels. In other words, the result of the neural interactions in, say, the medial geniculate, can conceivably be delivered both to the cerebral cortex and to stations that lie closer to the cochlea. Until further evidence from anatomy and physiology becomes available, however, the possible participation of the recurrent innervation in tonal perception must obviously remain entirely speculative.

A final matter is not so much a principle as an apology for the failure to uncover one. There is a large body of information on the comparative anatomy of the auditory system which has received no consecutive treatment here. It is entirely likely that a competent re-examination of this material would provide important clues to the problems at issue. The capacity for dealing with tones, as measured by psychological testing, is not remarkably dissimilar for fish, birds and men. Yet the neural endowment of these various forms is in many respects quite different. If, as is widely supposed, the structures with which man achieves his analysis of tones must operate also in the fish, bird and cat, then we can play down the importance, for example, of the dorsal cochlear nucleus and superior olivary region (these being reduced in man by comparison to the cat), the cerebral cortex (which is absent in the bird), and the cochlea itself (for the fish does not have one at all). The pertinent question which cannot be answered here is that of whether a common minimum neural equipment exists in all these forms that 'perceive' and discriminate tones.

PHYSIOLOGICAL CONSIDERATIONS

In a previous section the basic neural processes for pitch, as deduced from the data of psychology, were stated to involve a rather large portion of the auditory system, in particular ways, for rather long periods of time. The anatomical review has provided some conceptions of where and how this neural analysis of tones might occur. The objective of the present section is to assemble the available physiological evidence and build them into the conceptual framework already established.

The evidence to be cited has been collected largely through two types of experiments. There are, first, the extirpation experiments: pre-operative capacities of an animal are compared with performance after removal of a portion of the brain suspected to be necessary for the hearing process. Such studies are frequently—and probably best—done in animals unanesthetized at the time of testing. The second type of experiment, usually performed on anesthetized preparations, seeks to discover the details of the brain activity evoked when tones (or their equivalent) are presented to the ears. Electrical techniques for recording nerve action potentials are the main tool, and the studies with microelectrodes of the activity of single auditory neurons have during the past decade provided some of the most useful information. It is with these two kinds of experiments that we will be chiefly concerned here.

Problem of Localization. Since before the time of Helmholtz (10), and certainly during the past 100 years (166), a most persistent conception of the mechanism for pitch perception has been the idea that some unique spatial correlate exists for each perceived tone. As this idea was put by Helmholtz a sharply localized region of the basilar membrane (and of the associated auditory neural apparatus) was thought to be uniquely excited by each tone. More recently *time* has been added to *place* as a factor in conceptions of how the analysis of tones is achieved by the nervous sys-

tem. An almost endless variety of combinations and modifications of these two factors has been advanced as explanations (11, 166), it being by now generally conceded, even by some who once felt otherwise, that at least some tones are distinguished from one another because they produce their effects at different places. The principal unsolved problems appear to be in what way and at what times those places differ. We shall examine these questions in order.

Localization at the auditory nerve level. A few inspired guessers among the theoreticians have visualized low frequencies as arousing activity over all or much of the basilar membrane and its related neurons, with involvement of progressively smaller regions and fewer elements as the stimulus frequency increases. From the evidence to be presented now, it looks as if they may be right. Tasaki, in a report seen only in manuscript (154, 155), has obtained electrical records from single auditory nerve fibers in the guinea pig after surmounting the difficult technical problems involved. We are thus at last in possession of at least some of the basic facts of how these fibers behave when tones (between 500 and 9000 cps) are presented to the ear, and these are as follows. First, the principal difference between auditory nerve fibers is in terms of what tones they respond to. Some respond only to low tones, some to low and intermediate tones, and some to low, intermediate and high frequency tones. A particular fiber will, in other words, be activated by few, many, or (practically) all of the tones the animal may be expected to hear. Wherever the fiber has its high frequency limit, its sensitivity drops there very abruptly; one may say, therefore, that each auditory nerve fiber responds to all frequencies up to, but not beyond, its characteristic cut-off point. Tasaki infers, with good reason, that this cut-off frequency is the neural counterpart of a corresponding cut-off in the mechanical motion of the basilar membrane directly observed (7) and also deduced from cochlear microphonic studies (156).

Tasaki's second point is that auditory afferents show only excitation, never inhibition, in response to stimulation. In this regard they resemble the primary sensory neurons in the dorsal root and elsewhere, and differ from post-synaptic neurons in the cochlear nucleus (46, 49), the retina (57) and elsewhere, since inhibition of activity in these situations is a common consequence of sensory stimulation. Tasaki's observations were, however, made chiefly with tones of very brief duration, and the question of whether inhibitory effects might occur with tones of longer duration may perhaps still be considered as unsettled. Nevertheless, speculations that the efferent bundle described by Rasmussen and discussed above might modify the neural input from the cochlea by inhibition are clearly not supported by his results.

The final major point uncovered by Tasaki is that two populations of auditory fibers can be differentiated on the basis of response to intensity. One group of elements responds briskly to tones of moderate intensity, while another reacts less well. This fact he interprets as showing the fiber to be connected to external or internal hair cells, respectively. As discussed above, it has long been supposed that the internal hair cells have a higher threshold than the externals, and this finding would appear to support that contention.

These important results can be harmoniously related to a group of experiments in which the auditory nerve has been cut in both man and animal. In man, partial section of the auditory nerve incidental to cutting of the vestibular root to relieve symptoms in Menieres disease results in hearing loss post-operatively. In 78 such cases recently summarized (60), these patients, without exception, heard high frequencies less well after the operation. None suffered significant loss for lower tones.

The results in animals exactly parallel the observations on human beings (102, 166, 167). Partial section of the auditory nerve in cats also produces more or less loss at high frequencies only. In a discussion of such results, Neff (102) suggested that the difference between high and low frequency tones, in auditory nerve terms, might lie in whether few or many nerve fibers became excited. He supposed that high tones excited a small population of fibers, while progressively lower tones excited these plus others. Random destruction of neurons would thus be more likely to impair hearing for high tones, and if any fibers were spared, perception for low tones would be more likely to remain. Tasaki's results seem to agree very well with this formulation.

Before leaving Tasaki's results we should examine his findings with respect to the time relation between the stimulating wave and the neural impulses it arouses. This problem was examined with simultaneous recording of the cochlear microphonic response (basal turn) and the nerve fiber discharge. Tasaki found that at 290 cps all discharges tended to be distributed over a particular quarter of the sound wave cycle. At 500 cps, however, only about half the units (out of 22 studied) discharged during a particular quarter, while the rest were approximately equally distributed over the remaining three quarters of the sound wave cycle. Thus the important idea that synchronous volleys of auditory nerve impulses are aroused by low frequency tones (166) receives only indifferent support from these data. Synchrony is at best inexact at 290 cps, and considerably worse at 500 cps. A final decision on this important point, however, should perhaps await the accumulation of further data.

Localization at the medullary level. Microelectrode studies upon neurons in the cochlear nucleus demonstrate unequivocally that different tones produce different neural effects at this level in the nervous system (46, 48, 49, 61, 68, 69). Just as a particular auditory-nerve cell responds only to a limited range of sound frequencies, so too the neuron one synapse beyond shows a specific response to tones. Both display the sharp decline in sensitivity at the high-frequency limit of their response band; these are sufficiently similar in shape furthermore to permit the inference that the medullary neuron is to a first approximation simply reflecting the activity conveyed to it by the primary fiber.

Significant additional points relevant to the localization problem have emerged from the cochlear nucleus studies. Of these the most important is probably the existence of an additional cut-off region, this time at the low frequency end, for many if not most of the medullary neurons. The presence of this low-frequency cut-off is most clearly demonstrated in experiments where two tones are simultaneously presented to the ear (46); a remarkable restriction in the frequency band to which the unit responds is the result. This phenomenon is clearly traceable to the neural process of inhibition occurring, most probably, among the neurons of the cochlear nucleus itself. When only single tones are used the sensitivity of some cochlear nucleus units to tones of low frequency is much less than that of the auditory fibers studied by Tasaki. Whether this also is due to neural inhibitions remains to be settled. It is known, however, that tones just beyond the high-frequency cut-off point of a cochlear nucleus neuron may be extremely effective in stopping its spontaneous activity. This effect can probably only be produced through neural inhibition. Thus neural inhibition is to be assigned some place as a neural mechanism involved in the analysis of tones. How important its role will prove to be cannot of course be stated. We know only that at the cochlear nucleus a tone possesses, in addition to the capacity of activating certain neurons, the property of preventing

the excitation of certain others. The effects of a tone upon the cochlear nucleus must be visualized as creating regions where activity is increased as well as ones in which it is reduced or abolished. The creation of these separated islands of activity and inactivity is a distinctive neural contribution to the analysis of the tone, and their locations might well serve as a significant central cue to its frequency.

The cochlear nucleus studies reveal a second relevant fact, namely that the apparently precise anatomical projection ('unrolling') of the cochlea has its physiological counterpart. When a microelectrode is passed in very small stages through one of the cochlear nucleus regions within which different cochlear sites are projected, it encounters, in orderly progression, a changing sensitivity to frequency (51). Unfortunately relatively few of the 13 separate subdivisions of the cochlear nucleus have been explored systematically in this way, so that the generality of these findings remains in some doubt. Insofar as they go however, the results demonstrate a remarkable coincidence between the anatomical predictions and the physiological findings regarding where the excitatory effects of tones are to be found. One can confidently infer from this that if an abnormal neural pattern should arrive from the cochlea due to some deficiency there in the capacity of the basilar membrane to excite its associated neurons, this deficiency will be preserved at the cochlear nucleus level.

We lack information on a number of points germane both to cochlear neural events and to the way the cochlear nucleus processes its neural input. Many of these can be settled only by pure anatomical research that will provide a clearer understanding of the cochlear neurology. As an example it would seem only reasonable to suppose that the obviously different cochlear distribution of radial and external spiral fibers would be matched by some discernible difference in their central terminations also. Yet only one such central ending has been described, although it has been authoritatively stated that the possibility that other types might exist is to be left open (88, p. 337). A related anatomical point that presumably can be resolved is the important one of whether auditory nerve collaterals do or do not end in the dorsal cochlear nucleus (153).

On the physiological side it is interesting to consider certain implications of the anatomical facts. The extreme fineness and prolonged course of the external spiral fibers in the cochlea (some of which may measure less than a micron in diameter for a length of at least 3 mm.) means that a considerable amount of time must pass before impulses aroused in them reach the cochlear nucleus. If conduction in these attenuated fibers occurs as slowly as a fraction of a millimeter per millisecond it is conceivable that before impulses have made their tortuous way from hair cell to medulla in the external spiral fiber system the cortex has already been aroused by impulses originating in the more direct radial fiber system. On the other hand, since the normal basilar membrane is a very broadly tuned structure (7, 8) it is not unreasonable to suppose that the entire length of an attenuated external fiber might frequently be almost simultaneously excited. The hair cell that lies closest to the point of entry of the neuron into the modiolus would then be the one to evoke the nerve impulse which, in addition to passing centrally, would pass also into the peripheral prolongation. Such complications as these make for unique properties attributable to the external spiral fibers as compared to the radial ones; it seems therefore likely that Tasaki's conclusions that they can be differentiated on the basis of the stimulus energy required for excitation represents only one of many functional differences that eventually will be defined.

With respect to events in the cochlear nucleus it is necessary again to raise the matter of the efferents to the cochlea. If these should selectively inhibit and facilitate action in the afferent fibers, as originally conceived by Herrick (67, p. 75), events at the cochlear nucleus would be divisible into those that occur before, and those that occur after, the action of the efferents took place. The formal similarity between this problem and that raised by the motor innervation to sense organs in the muscle (78) is apparent. One must also bear in mind that in its structure the dorsal cochlear nucleus resembles the cerebral cortex while the ventral nucleus clearly does not. The premise that these two major subdivisions of the cochlear nucleus complex perform different functions is defensible despite the almost complete absence of physiological support for it.

A need for further precise information about the behavior of the medullary neurons may, finally, be cited. There is, for example, the matter of their 'spontaneous' activity. First described for

elements in the cochlear nucleus (46, 48), 'spontaneous' discharge has subsequently been found to occur in a substantial number of the units isolated with microelectrodes in every auditory tract and nucleus so far studied. Since one of the two prominent actions of a tonal stimulus is to abolish some of this 'spontaneous' activity, efforts to understand the physiological basis for its production and abolition, and more adequate data on what cells show it and what do not would certainly appear to be in order. Considerable emphasis has also been placed in this discussion upon the cut-off frequencies of the auditory neurons; this is natural, for by far the majority of units thus far studied displayed this feature. However, some trapezoid neurons do not (69) and units exceptional in this and other ways have also been described (46, 48). The size of these exceptional populations will have to be determined and a more exact description of their deviant behaviors will be required before any conceptualization of the neural basis for tone perception can be seriously entertained as an explanation.

Localization at higher neural levels. Evidence for localization similar to that just described has been obtained through microelectrode studies at the inferior colliculus (158) and medial geniculate body (47, 58). Most units isolated at these various levels are activated by certain tones and suppressed by others. Unique drops in sensitivity at both the high and low limit of the frequency band causing response show them to resemble cochlear nucleus neurons in their behavior. The degree to which these cut-offs simply reflect the activities in earlier stations rather than result from interactions within the nucleus under study has not been settled. There is general concern that the conditions of anesthesia under which such experiments are performed may significantly interfere with the processes under study (41, 47 p. 397, 58 p. 411). For a discussion of other special problems and properties of the auditory neuron at higher levels the reader is referred to the original papers.

Systematic microelectrode studies upon the auditory cortex have not yet been reported; technical problems of considerable magnitude remain to be effectively solved. Results derived with other techniques, however, argue strongly that each tone activates only a restricted group of cortical cells. Thus the strychnine technique discussed earlier (70, 163, 164) and the Laplacian recording method (50), both show the cells within a small cortical focus to be sensitive to certain tones only; furthermore, a plot of the tones to which response is recorded always shows the familiar cut-offs at high frequencies and often at low frequencies as well.

For the higher neural stations, therefore, the available physiological evidence, while relatively meager, is on the whole consistent with the general concepts developed from the analysis of the cochlear nucleus. Restricted responsiveness to tones is observed whenever a unit or small group of units is studied; and when the responses of many units at a particular station are tabulated they are found approximately to cover the range of heard tones (with the possible exception of very low tones). From this one must deduce that a tonotopic organization exists within the auditory nervous system. Presumably this tonotopic relation bears a close relation to the underlying anatomical topologic one, but whether this is so cannot be satisfactorily settled until the details of both are better understood.

Localization in the light of extirpation studies. If the topologic projection of the cochlea should have important functional consequences in the perception of tones, it follows that small local lesions in an auditory nuclear mass should interfere with the hearing of certain tones only. This simple idea has dominated considerable research upon the hearing of animals and man. Only a few of the high points of the body of accumulated evidence can be treated here.

In cats a lesion restricted to the apical turn of the cochlea significantly raises the threshold of low frequency tones only (140). This report of the effect of local

cochlear lesions upon tone perception is merely one of a long series of such from which various investigators have concluded that low, middle and high tones exert different local effects upon the basilar membrane. Experimental lesions of many types, including those produced by excessive stimulation (e.g. 27) have been employed in this type of research; for a cogent summary of this material the reader is referred to the work of Wever (166, pp. 199-220).

When the cochlear nerve is cut, the result (60, 102, 167), as discussed earlier in another connection, lends support to this general idea that different tones are functionally differentiated in terms of which nerve fibers are activated in the cochlea. A critical evaluation of the consequences of subcortical lesions other than those in the auditory nerve upon hearing behavior is impossible at this time, for the appropriate experiments seem yet to be made (but see 3, 77, 122).

With respect to the auditory cortex, the effects of lesions are somewhat better understood. Surgical removals in dog (5, 56, 86), cat (32, 94) and monkey (38) have been reported to have remarkably little effect upon the detection of tones and the learning and retention of even very fine discriminations between them. In the cat AI, AII, Somatic II (which contains AIII), and Ep must be removed before the simple discrimination between tones (near 1000 cps) is permanently lost (94); an animal with such a lesion, furthermore, can still be taught to respond to a tone. In other hands (20) a similar lesion did not prevent the post-operative relearning of a fine discrimination. The only lesion that clearly abolishes the discrimination habit and precludes its being relearned is a widespread removal that spares only the motor region and frontal cortex. In monkeys, auditory cortex removals that produce degeneration of 90 per cent of the medial geniculate fail to interfere with the relearning of a pitch discrimination or with its retention (38). The evidence is therefore clear that tonal discrimination of a precise nature is still possible when the cortical termination of the classical auditory pathway is very severely damaged. Surprising as it may be, the auditory areas of cat (AI, AII, Ep), dog and monkey seem not to be particularly necessary for the learning and retention of a delicate frequency discrimination. Furthermore, if cerebral cortex is involved in this function, it can lie outside what is generally conceded to be primarily auditory.

Before analyzing these results further it will be well to consider the recent results of Diamond and Neff (32) on the effects of cortical removals when auditory patterns were used as test stimuli. Two tones, *A* and *B*, were employed; the animal was required to respond when the pattern changed from *ABA* to *BAB*. The cats readily learned this task pre-operatively but, after bilateral cortical lesions (AI, AII, and Ep), they lost the ability and could not relearn it. Like the equivalent animals of Meyer and Woolsey, however, they learned to make appropriate responses to a simple change in frequency post-operatively. After auditory lesions that spared only a part of AII the pattern discrimination was lost but could be relearned. No loss whatever ensued when only most of AI was removed. Thus even for the relatively complex problem of dealing with simple tonal patterns AI is not necessary, although AII and Ep apparently are. Firm conclusions on all these points are not yet justified by the data, but auditory cortex other than AI is clearly implicated for perception of tonal patterns, while little if any of the so-called 'auditory cortex' seems to be required for simple discrimination of tones.

This fact that AI, the region to which the medial geniculate projects and within which the cochlea is unrolled, appears to be completely unnecessary for the performance of tasks in which tones are the discriminanda must come as a surprise to

most auditory physiologists. It has long been supposed that AI played an important part in all situations, even the simplest ones, where tone frequency discriminations were of importance to the animal. The strong suggestion that it does not forcefully poses the question of what functions, presumably complex ones, it actually does subserv. In addition these results clearly indicate that subcortical auditory mechanisms can perform a completely adequate analysis of the tonal stimulus, that they make important connections not only with auditory but also with extra-auditory cortex, and that the extra-auditory cortex makes a significant contribution to the performance of auditory tasks. It would appear, in other words, that interactions important for the mediation of tone responses occur in neural tissue other than what has hitherto been considered to be primarily involved.

Factor of Time. In the preceding paragraphs the physiological evidence upon where neural events occur in response to tones has been collected. Since it is generally agreed that temporal features are also involved in the analysis of tones, it is proposed to discuss here briefly what these might be, and to describe some that are known.

If a steady tone is presented on the subject he experiences a sensation that has a definite onset and a duration. It might therefore be expected that among the neural events discoverable in the auditory tract one would be related to the onset of stimulation and another to its steady state condition. Certain studies on animals and men have uncovered neural correlates for both of these temporal aspects of tonal perception.

Onset responses of two types, differentiated on the basis of their latency, have been reported. Responses having short latency are recordable at all levels in the auditory pathway, the actual interval between the onset of a tone and the beginning of the response to it being approximately equal to that observed when click stimuli are used (2). At the medial geniculate bodies the onset response has been compared in detail to the electrical activity aroused by a click with the conclusion that during the first 20 msec. or so they are practically indistinguishable from one another both in latency and in shape (47). This fact suggests that the arousal of a relatively nonspecific neural response may be the first consequence of tonal stimulation, and that the distinctive neural events required to differentiate tones from any other type of sound emerge only after a time interval to be measured in tens of milliseconds has elapsed. This point, which can hardly be said to be firmly established, raises a matter of considerable theoretical importance. Practically all of the cortical experiments in which tones were used to evoke electrophysiological responses utilized this onset response exclusively as the primary datum (e.g. 50, 81, 164). It is a universally recognized fact that when large electrodes are used for recording, tones can be relied upon to arouse the onset response only, and little further activity is ordinarily evoked from anesthetized preparations. If this onset response should prove to be less of a specific index of tone frequency than merely the signal that a sound has occurred, the tonotopic organization shown in current cortical maps, insofar as this rests upon electrophysiological data, is subject to obvious revision.

At the cortex, in animals, the onset responses of short latency just discussed occur at around 10 msec. after the tone is turned on. Another category of onset responses having much longer latencies (of the order of 50-400 msec.) is recordable from the cortex of both animals (85) and men (29, 116). It is tempting to postulate that the short latency responses are conducted by way of the classical afferent pathway while those with long latency reach the cortex by way of the reticular activating pathway (*vide supra*). Some evidence can be adduced for this formulation (85), but

at the present time no definitive explanation for the two types of onset responses appears to have been made.

Steady state responses toward tones have been described at subcortical and cortical levels. As has already been discussed, microelectrode studies (46-48, 58, 68, 69, 155, 158) show single neurons in the subcortical nuclei and tracts to respond in a stable way during the presentation of tones. Except in the auditory nerve the stable change induced is a reorganization of neural activity in which some neurons are aroused to brisk action while the activity of others (including the 'spontaneous') is reduced or abolished. In the auditory nerve only excitation is produced. When the tone goes off, its specific neural effects disappear, but these can be reinstated by turning the tone on again. If the frequency of stimulation is changed, the populations of neurons that undergo excitation and inhibition change correspondingly. This production of localized islands of neural excitation and inhibition, in different places for different tones, is at the present time the best demonstrated functional correlate we possess for the steady state of tones

This generalization has been synthesized from the fragmentary and incomplete reports already cited on the nature of the response of single units at various levels of the auditory system. By their nature such studies begin by attending to the effects of tones upon a particular neuron, *A*. The electrode position is then changed and the behavior of a second neuron, *B*, is examined using the same stimuli. The process continues until the largest possible number of neurons has been isolated and studied. A basic unproved assumption is that if a particular tone activated neuron *A* but inhibited neuron *B*, this situation existed throughout the whole of the experiment, and, indeed, that it existed before the animal was even brought to the laboratory.

The flimsy threads from which the generalization is made could be appreciably strengthened by further evidence along the following lines. The existence of both active islands and islands of suppressed activity can be taken as demonstrated, but their extensiveness in the anatomical sense, the number that are created by a given tone and the spatial relations between them are impossible to assess with the present information. Studies with multiple microelectrodes through which activity can be sampled simultaneously at many loci within a given nucleus should provide useful answers. Such studies could also reveal the temporal course of the development and decay of the activity characteristic of a particular group of cells. With respect to the latter it is known at present only that auditory units driven (or inhibited) by tones show adaptation to the stimulus. They tend, if activated, to show a decline in discharge frequency with time, and they may adapt to extinction within a matter of seconds (48, 158); if the action of the tone is to suppress discharge, this effect too tends to disappear after the tone has been on for some time (48). These observations suffice only to indicate that the decay of neural events caused by tones is some function of time, but they provide little in the way of useful detail. On the related question of how neural activity builds up following the stimulus onset even less can be said. Thus the dynamics of the relationship between tone and its neural effects are still largely unknown although the evidence that such dynamics exist is unequivocal.

The search for correlates for the steady state at the cortical level has to a large extent been unsuccessful, and for such information as we do possess we have to thank those who have used unanesthetized preparations. Bremer (15-18) has shown sustained activation of AI (for a second or longer) by tones ranging between 300 and 5000 cps in both the sleeping and waking cat. The response consists of a train of electrical oscillations whose frequency rises (up to about 70/sec.) as intensity increases; these waves tend to disappear with time but are restored by either a slight change in frequency or a brief period of silence. The only tonal stimulus known to produce continuous cortical activity over a period of minutes has been described by Whitfield (168). This is a tone whose frequency is varied so as to produce the effect of a very slow vibrato. The frequency modulation amounts to a few per cent, its rate being about 1/sec., and intensity is regulated to remain constant throughout.

Records of the cortical response of cat *encephale isolé* preparations to this stimulus show a regularly repeating pattern at the modulation rate. The results of further studies with this stimulus—unique insofar as its effects are concerned—are to be anticipated with interest.

In Bremer's study, areas adjacent to the activated auditory cortex may show a concomitant decline in activity. Thus, again, a pattern of excitation and inhibition is the consequence of a continued tonal stimulus, a point worth mention despite the obvious fact that the cortical experiment, on auditory and extra-auditory regions and utilizing large electrodes, is not comparable to the subcortical experiments, which used microelectrodes within regions presumably exclusively auditory in function. Nevertheless, at the cortex too the steady state condition (up to a few seconds at least) has as one of its correlates a pattern of neural excitation and inhibition with a particular distribution in space.

The experiments just cited represent practically all that is known about the temporal course of the neural response to tones. Before concluding discussion of this factor of time, however, it will be well to deal briefly with certain theories of hearing, both old and new, in which time plays a major role. A scholarly summary of most of these, along with a detailed exposition of the so-called volley theory in its modern form, has recently been published (166). Volley (or frequency) theories of hearing postulate a precise timing between the frequency of nerve discharges and the frequency of the tone that evokes them. They rest therefore upon a simple assumption that is subject to experimental test. As we have just seen, the experimental evidence on this point is still somewhat scattered and incomplete. Data obtained with microelectrodes at the auditory nerve (154, 155) and cochlear nucleus (46, 48) levels leave no doubt that a relationship does indeed exist between the stimulus frequency and nerve response frequency. This relationship, however, is not precise, even for frequencies as low as 300 cps in auditory nerve fibers. At the inferior colliculus and medial geniculate levels the evidence at hand is not particularly useful, but what we have makes it also seem unlikely that response frequency can be precisely related to that of the stimulus when anesthetized cats are subjects. Nevertheless, the following statement made by Professor Wever is unquestionably correct: "Every neural element relays two sorts of information, the position along the membrane that it serves and the periodicity of its excitation" (166, p. 440). At the present state of our knowledge it would clearly be unwise to suppose that information conveyed in terms of periodicity of discharge, however poor it may prove to be, is rejected by the central nervous system. On the other hand it would seem equally unwise to cite this periodicity as of use only for perception of low tones. And, finally, it must be conceded that this periodicity may eventually be found to be no more significant for audition than for any other sense (like that of vibration) where the stimulus repeats in a regular and periodic manner. Thus the periodicity displayed by auditory neurons can be variously invoked and interpreted. At the present time no compelling neurophysiological evidence for or against a frequency theory of hearing exists, and the problem will only be settled through further experiments upon the nervous system.

Turning now to a significant recent trend in auditory theorizing—the attempt by physicists and mathematicians to apply their special techniques to the pitch problem—Licklider's views (151) will serve admirably as an example. He focuses attention on the interdependence of frequency, time and intensity in the analysis of any stimulating sound and points out that the human auditory brain, like any analyzer, must strike a compromise between analyzing the frequency and the time

features of the train of waves heard as a pure tone. What this compromise might be is the subject of a series of further papers (71, 80) in which two 'basic principles' of neural organization prove to be fundamentals for the argument. The first of these is "the principle of sloppy workmanship . . . (which) . . . states that it is dangerous to postulate a neural structure that is precisely arranged in detail. . . . One of the basic facts of neurophysiology is that the nervous system works despite a considerable amount of misarrangement of detail." This may be interpreted to mean, in part, that the exact behavior of single neural units is less important to know than some statistical aspects of their group behavior. The second is the "principle of diversity. . . . Instead of presenting a single transform of the peripheral stimulation to the higher centers, the auditory tract may present a number of transforms. Given a number of views of the stimulus, the cortex may look them over and take the most useful one. Or it may accept them all, trying to piece together a consistent picture of the outside world." In this view "the nervous system is the product of a superb architect and a sloppy workman." The architect, impressed by the need to get the job done, has provided parallel mechanisms by which it may be done. Idiosyncratic behavior of certain units or the absence through trauma or disease of all associated with a particular mechanism cannot completely deprive the organism of adequate contact with its environment. In thus providing parallel routes and alternative ways for analysis of the incoming message the nervous system, like all effective communications systems, stresses redundancy; and it operates in a statistical and analogical way.

The paper dealing specifically with the parallel mechanisms at work in a nucleus like the cochlear nucleus (80) conceives pitch perception to result from a combination of both place and time analyses performed within the population of neurons. The place concept is the familiar one in which a particular tone is converted at the cochlea into a particular spatial pattern of nerve impulses that is preserved as a consequence of topologic projection. The time analysis is conceived to be an autocorrelational analysis. The signal from a local region of the cochlea is transmitted through more than one neural chain, thus suffering varying amounts of delay. Both delayed and nondelayed signals ultimately converge upon the same neurons where the further operations required for autocorrelation, namely multiplication and running integration, occur through the physiological processes of spatial and temporal integration at the synapse. The outcome is a temporal pattern of neural action, the result of a running autocorrelational analysis. Either this, or the analysis based on the topologic projection of the cochlea, or both combined provide the mechanisms by which tone frequency might be analyzed centrally. Such formulations are of some interest because they relate the recent advances in communications engineering to what is known about auditory physiology and anatomy; these efforts cannot fail to provide the stimulus for fresh and possibly profitable new experiments upon the auditory system.

Recapitulation. The auditory nerve has been called the bottleneck of the auditory system, for all the information the central nervous system can possibly obtain about environmental sounds is somehow encoded here in the discharges of a population of some 30,000 nerve fibers. A precise description of the space and time features of this discharge pattern evoked by a tone, and the changes that occur in it when tone frequency is varied, constitute the first step in the analysis of the neural mechanism by which the frequency of tones is mediated by the central nervous system. The single body of experiments that deal directly with this problem (154, 155) has yielded the following points. A tone activates (never inhibits) the neurons in the

auditory nerve, and the number that becomes activated is related to the frequency of the stimulating tone. The higher the frequency, the fewer the active fibers. It is further evident that with the rise in frequency the fibers that drop out do so abruptly; the fiber population that has just dropped out and that which will do so with a slight additional rise in frequency lie close together at their functional origins upon the basilar membrane. Thus the basilar membrane locus where mechanical disturbance changes rapidly from zero to its maximum is conveyed to the central nuclei as a distinction between closely adjacent regions of neural activity and inactivity. This is the summary of the unique spatial feature of the auditory nerve pattern, insofar as one is possible with our present limited information.

With respect to its temporal features little can be said. It is known that a tone arouses nerve response within about a millisecond of its onset, but any analysis of the subsequent course of events, with one exception, remains to be done. This exception deals with the steady-state frequency synchrony between the stimulating sound wave and the nerve discharges it arouses. This synchrony, in the anesthetized guinea pig, is not precise, but for tones up to perhaps 1000 cps some fibers at least appear to be driven at a submultiple of the stimulus frequency.

Turning now to the higher centers, the events at the cochlear nucleus must serve as our model despite the fact that scanty data are available regarding even its behavior. One point however is clear. The orderly topologic projection of the basilar membrane into this nuclear mass has its physiological, or tonotopic, counterpart. Both anatomical and physiological evidence agree that a place upon the basilar membrane can be precisely related to a place in the cochlear nucleus, and furthermore, there is good agreement among them as to the details. At higher nuclear stations a point-to-point projection is less firmly established by the methods of both disciplines, but the weight of the combined evidence is clearly in favor of the concept.

The microelectrode analysis has revealed that three categories of neural events can occur at a given place within the confines of an auditory nucleus where the cochlea is anatomically unrolled. With presentation of a tone to the ear, an auditory unit located at that place may be aroused to greater activity, it may show less than its customary activity, or its behavior may exhibit no appreciable change. Generalizing from this fact about what goes on at a particular place to what must go at various places in a structure like the cochlear nucleus, it seems evident that a particular tone produces excitation in some cells, inhibition in others, and no change whatever in still others. The spatial configuration of inactivated, activated, and unaffected loci thus created is probably unique for each heard tone. The central consequence of a tone acting upon the basilar membrane, therefore, is to differentiate a region where the cochlea is unrolled into clumps, or islands of cells where excitation and inhibition coexist simultaneously with adjacent unaffected regions. This way of looking at the neural effects of tonal stimulation differs significantly from previous so-called place theories only in that the places where nothing happens as well as those where inhibition occurs are specifically included as equal in importance to those where excitation takes place.

If one central correlate for the pitch experience is the place in the brain where neural effects are produced, correlates for other aspects of the pitch experience, like its slowness to develop, may eventually be revealed by study of the temporal course (development, duration and decay) of those same events. Unfortunately we possess at present so little information upon such matters that no reliable conclusions can be drawn.

One final matter deserves mention. Both anatomy and physiology show that auditory impulses penetrate the brain not only through the classical afferent pathway, but by other routes as well. An analysis, but not necessarily the same analysis, can be presumed to be occurring in all such paths. Furthermore, some central nuclei are clearly subdivisible upon anatomical grounds into different regions, like, say, those where collateral as opposed to terminal synapses predominate. The inference is certainly justified that the analysis occurring in each of such subdivisions will in some important respects be different. We have nothing as yet except speculations as to what those differences might be. Until more evidence is accumulated it would clearly be hazardous to postulate that any known mechanism for the neural basis of pitch perception is the only one, or even the most important one, at work.

SUMMARY

An attempt is made herein to assemble the material relevant to the question of how we come to hear tones. The detection and discrimination of tones, which in man culminate in the pitch experience, are functions to be explained through the synthesis of data provided by psychology, neuroanatomy and neurophysiology. From work on man and animals the psychologist defines the scope of the problem, suggests avenues of approach to the other disciplines and lays down certain constraints to theorizing. Their studies on lower forms reveal, for example, that neither a refined cochlea nor a highly developed auditory nervous system is prerequisite for adequate or even superior performance toward tones. Mammals deal with tones about as effectively as do birds, and so those elaborate anatomical refinements that uniquely distinguish the mammalian auditory apparatus probably neither hinder nor help in performance, and may actually be immaterial to the central issue. Studies on man reveal, furthermore, that possession of the requisite receptive and neural apparatus does not guarantee perception of and discrimination between tones. To hear we must 'listen,' and intelligent adults, who at first cannot tell one tone from another, can be 'taught' to do so. Thus attention and learning and their neural mechanisms (about which little can, at present, be said) must play a significant if still poorly understood role in the hearing of tones.

The review presents also a summary of the anatomy of the auditory nervous system. The 'wiring-diagram' that charts the routes by which auditory signals impress themselves upon the brain becomes increasingly more complex as new information accumulates. In addition to the classical afferent pathway shown in most textbooks, and discussed nucleus by nucleus in this review, auditory connections involving the cerebellum and the reticular formation have recently been defined. Furthermore, a system of neurons descends from cortex to medulla, possibly having as its final link the olivo-cochlear pathway that is known to end in the region of the internal hair cells.

A discussion of such physiological correlates for tonal frequency as have been uncovered by animal experimentation is given also. The role of cerebral cortex and subcortical structures is evaluated in the light of extirpation studies. There is clear evidence to oppose a contention that the auditory areas of the cerebral cortex are required for simple perception and discrimination of tones, for when such areas are removed in animals, their performance is only minimally altered. The cortex may, however, be implicated in the learning and retention of behavior conditioned to patterns of tonal stimuli. As for subcortical structures, the evidence here is scattered, incomplete and difficult to evaluate.

The contribution of electrophysiological methods, in particular the results of

microelectrode studies, is examined with the aim of synthesizing generalizations about the neural mechanisms of tonal perception. At the auditory nerve level all fibers are activated by a band of tones, but at some high frequency the sensitivity of each drops, or cuts off, abruptly. Since these cut-off frequencies vary from one fiber to the next, it can be inferred that in terms of auditory nerve impulses, the difference between low and high frequency tones is the difference between many and few active neurons respectively. The mechanical events at the cochlea determine which specific neurons will be excited; high frequency tones excite their few neurons at the base of the organ, while low tones activate their many elements spread along the whole of the basilar membrane. The fact that indifferent synchronism exists between the sound wave and the auditory nerve impulse aroused by it, even for low frequency tones, constitutes evidence against the idea that frequency of nerve discharge is of crucial importance in the central mediation of tones.

The spatial correlate for stimulus frequency imposed upon the system by mechanical events at the cochlea and reproduced in the nerve is preserved at the cochlear nucleus level. A tone here may result in excitation or inhibition of a particular neuron, or it may have no effect upon it at all. A neuron activated by tones is sensitive to a limited number of them and, like its neural predecessor, it shows a cut-off point at the high-frequency end of its range. In addition, abrupt changes in sensitivity may occur at low frequencies or elsewhere, and when they do they result, in most instances if not in all cases, from neural inhibition.

The established spatial correlate for frequency, taken together with the fact that a tone excites some and inhibits other neurons at this level, can be supposed to create islands of neural activity and suppression interspersed among islands of unaffected neurons, the whole configuration being unique for each heard tone. Studies at higher neural levels, insofar as their results are applicable, do not contradict this concept of neural mechanism to mediate tones. If such islands exist, their number and distribution, the temporal course of their development and decay, and the nature of the interactions that produce them all remain to be settled. In spite of the many uncertainties, no other neural correlate of tonal stimulation has at the present time as many points in its favor as this modified 'place' concept. The question of how a locus of neural action becomes converted into a particular sensation is one that hearing shares with the other senses; we do not yet possess the answer.

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